CLAIMS

1. A method of synthesizing a block copolymer, said method comprising the steps of:

(a) providing a first compound comprising a polymeric thiol precursor;

(b) generating a polymeric thiol from said first compound; and

(c) initiating a polymerization of a second compound comprising an episulfide group with said thiol produced in step (b) thereby producing a block copolymer comprising a terminal thiol.

2. The method of claim 1, said method further comprising step (d) end-capping the product of step (c) with a third compound that comprises a group that is reactive to thiols thereby producing a block copolymer comprising at least three blocks.

3. The method of claim 1, said method further comprising step (d) using said terminal thiol from the product of step (c) in a second polymerization step.

4. The method of claim 1 or claim 2, wherein said first compound further comprises a hydrophilic polymer.

5. The method of claim 4, wherein said hydrophilic polymer is selected from the group consisting of poly(ethylene oxide), poly(ethylene oxide)-co-poly(propylene oxide), poly(N-vinyl pyrrolidone), poly(ethyloxazoline), poly(acrylic acid), poly(ethylene-co-vinyl alcohol), poly(acrylamide), poly(N-alkyl or N,N-dialkylacrylamides), poly(acrylates), poly(peptides), and poly(saccharides).

6. The method of claim 5, wherein said hydrophilic polymer further comprises polar, ionic, or ionizable groups.

7. The method of claim 1 or claim 2, wherein said first compound further comprises polyether or a block copolymer, wherein at least one block comprises polyether.

8. The method of claim 7, wherein said polyether comprises a molecular weight of > 300 Da and a terminal, electron-poor double bond.

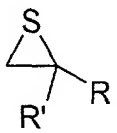
9. The method of claim 7, wherein said polyether is poly(ethylene glycol).

10. The method of claim 1 or claim 2, wherein said first compound further comprises a peptidic sequence or a saccharidic sequence.

11. The method of claim 1 or claim 2, wherein said polymeric thiol precursor is selected from the group comsisting of a thioester, a dithioester, a thiocarbamate, a dithiocarbamate, a thiocarbonate, a xantate, and a trithiocarbonate.

12. The method of claim 1 or claim 2, wherein said first compound comprises a linear, star-shaped, or branched polymer with a thiol precursor at each end.

13. The method of claim 1 or claim 2, wherein said episulfide in step (c) comprises



where R or R' comprises hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, phenyl, substituted phenyl, acyl, or carboxyalkyl.

14. The method of claim 2, wherein said third compound comprises polyether or a block copolymer, wherein at least one block comprises polyether and a Michael acceptor group or a leaving group capable of being displaced by a nucleophilic sulfur atom.

15. The method of claim 14, wherein said polyether comprises poly(ethylene glycol).

16. The method of claim 14, wherein said Michael acceptor is selected from the group consisting of acrylate, itaconate, acrylamide, itaconamide, maleimide, vinyl sulfone, quinone, multi-substituted quinone, fused quinone, vinyl pyridine, and vinyl pyridinium ion.

17. The method of claim 14, wherein said leaving group is selected from the group consisting of chloride, bromide, iodide, tosylate, mesylate, bromoacetate, iodoacetate, substituted and unsubstituted benzyl bromide, bromoacetamide, iodoacetamide, and triflate.

18. The method of claim 2, wherein said third compound comprises a compound having a low molecular weight and a group with Michael-type reactivity or a group capable of undergoing nucleophilic substitution.

19. The method of claim 18, wherein said third compound further comprises a functional group selected from the group consisting of peptide, ester, anhydride, and Schiff base, and acetal.

20. The method of claim 2, wherein said third compound further comprises a block copolymer comprising a group that undergoes hydrolytic degradation.

21. The method of claim 20, wherein said group is selected from the group consisting of aliphatic ester, anhydride, Schiff base, and acetal.

22. The method of claim 2, wherein said third compound is the product of step (c).

23. The method of claim 1 or claim 2, wherein said second compound comprises a compound selected from the group consisting of propylene sulfide, cyclohexene episulfide, and ethylene sulfide.

24. The method of claim 1 or claim 2, wherein the step (c) further comprises adding a fourth compound comprising an episulfide group.

25. The method of claim 24, wherein said third compound is added simultaneously with said second compound to produce a random copolysulfide.

26. The method of claim 24, wherein said third compound is added sequentially before or after said second compound to produce a block copolysulfide.

27. The method of claim 1 or claim 2, wherein the conversion of the thiol precursor to a thiolate in step (b) comprises a transesterification or transamidation reaction.

28. The method of claim 2, wherein said third compound is thiirane.

29. The method of claim 2, wherein said third compound further comprises a peptidic sequence or a saccharidic sequence.

30. The method of claims 10 or 29, wherein said peptidic or sacchardic sequence comprises a peptide or a saccharide that binds to an adhesion-promoting receptor.

31. The method of claim 30, wherein said peptidic sequence comprises RGD or YIGSR.

32. The method of claim 10 or 29, wherein said peptidic sequence comprises a proteolytically degradable sequence.

33. The method of claim 32, wherein said proteolytically degradable sequence comprises a substrate for a protease selected from the group consisting of plasmin, elastase, collagenase, and a matrix metalloproteinase.

34. The method of claim 2, wherein said third compound comprises a polymeric backbone identical in chemical nature to said first polymer.

35. A dispersion comprising a product of the method of claim 1 or claim 2 and water.

36. The dispersion of claim 35, wherein said dispersion further comprises a self-assembled aggregate of said product of the method of claim 1 or claim 2.

37. The dispersion of claim 36, wherein said self-assembled aggregates comprises a structure selected from the group consisting of spherical micelle, worm-like or cylindrical micelle, lamellar structure, and other lyotropic structure.

38. The dispersion of claim 36, wherein said self-assembled aggregate comprises a vesicle comprising one or more lamellae.

39. The dispersion of claim 36, wherein said dispersion further comprises a pharmaceutically acceptable formulation.

40. The dispersion of claim 36, wherein said self-assembled aggregate further comprises a drug.

41. The dispersion of claim 40, wherein said drug is attached to said self-assembled aggregate by a hydrolytically degradable linker.

42. The dispersion of claim 36, wherein said self-assembled aggregate further comprises a targeting moiety immobilized on a surface of said self-assembled aggregate.

43. The dispersion of claim 42, wherein said targeting moiety is selected from the group consisting of heparin, a heparin-binding moiety, a growth factor, a growth factor receptor-binding moiety, a cell-surface receptor-binding moiety, a DNA-binding moiety, an RNA-binding moiety, an adhesion-promoting branched saccharide, an antibody or portion thereof, a nucleic acid, a nuclear localization sequence, a pathogen mimetic, proteoglycan-binding peptides and ligands, an organic ligand, an adhesion peptide, a peptidomimetic, a saccharide, and a combinatorally-discovered peptide.

44. The dispersion of claim 43, wherein said growth factor is selected from the group consisting of aFGF, bFGF, VEGF, BMP, and TGF.

45. The dispersion of claim 36, wherein said product of the method of claim 1 or of claim 2 comprises hydrophilic and hydrophobic blocks that are experimentally optimized to produce self-assembled aggregates that escape recognition by the body's mechanisms of vascular particle clearance.

46. The dispersion of claim 36, wherein said self-assembled aggregate is stable at pH 7.4 and destabilized at pH < 7.4 or pH > 7.5.

47. The dispersion of claim 39, wherein said dispersion further comprises an excipient.

48. The dispersion of claim 47, wherein said excipient is selected from the group consisting of a membrane permeabilizing agent and a drug stabilizer.

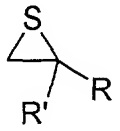
49. The dispersion of claim 36, wherein said self-assembled aggregate comprises a proteolytically degradable sequence that influences a stability of said aggregate.

50. The dispersion of claim 46, wherein said self-assembled aggregate further comprises a compound selected from the group consisting of imidazole, histidine, phenol, and tyrosine.

51. The dispersion of claim 36, wherein said self-assembled aggregate further comprises a hydrolyzable group selected from the group consisting of anhydride, ester, acetal, and Schiff base.

52. The dispersion of claim 36, wherein said self-assembled aggregate comprises a linear polymer comprising a hydrophilic block and a hydrophobic poly(episulfide) block.

53. The dispersion of claim 52, wherein said hydrophobic poly(episulfide) block comprises a polymerization of a compound comprising:



where R or R' comprises hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, phenyl, substituted phenyl, acyl, or carboxyalkyl.52. Micelles formed from linear polymers that comprise a hydrophilic block and a hydrophobic poly(episulfide) block.

54. The dispersion of claim 52, wherein said self-assembled aggregate comprises a micelle.

55. The dispersion of claim 53, wherein said self-assembled aggregate comprises a micelle.

56. The dispersion of claim 52, wherein said self-assembled aggregate comprises a vesicle.

57. The dispersion of claim 53, wherein said self-assembled aggregate comprises a vesicle.

58. The dispersion of claim 36, wherein said self-assembled aggregate degrades by oxidation under physiological conditions.

59. The dispersion of claim 40, wherein said self-assembled aggregate degrades by oxidation of a sulfur atom under physiological conditions thereby releasing said drug.

60. The dispersion of claim 40, wherein said self-assembled aggregate comprises a micelle.

61. The dispersion of claim 40, wherein said self-assembled aggregate comprises a vesicle.

62. The method of claim 2, further comprising a step (e) reacting a fourth compound with a terminal thiol of the product of step (d).